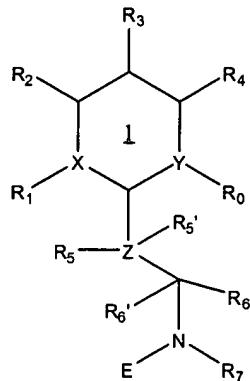


LISTING OF CLAIMS

This listing of claims will replace all prior versions, and listings, of claims in the application. In amendments to the claims, additions are represented by underlining and deletions are represented by ~~strikethrough~~ or, in cases of five characters or fewer, by [[double brackets]].

1. (currently amended) A hydrophilic transportable dopaminergic prodrug compound according to FORMULA V,



Formula V

wherein,

Ring 1 comprises an aryl or heteroaryl ring having has 4 to 8 carbon atoms, among which atoms are counted "X" and "Y";

each of X and Y is optional; X, when present is either a carbon atom, -C(R₁)₂- or -C(R₄)₂- - (CR₁)₂-; Y, when present, is either a carbon atom, -CH₂- or CH₂-CH₂-;

z, R₅ and R₅' are optional, and when present z, R₅ and R₅' together form a lower alkyl or a substituted lower alkyl moiety;

N is part of either an amine or an amide linkage;

E is a saccharide which forms a linkage with N through a single bond from a carbon or oxygen atom thereof;

R₀ is hydrogen;

R₁ and R₄ are selected from the group consisting of hydrogen, hydroxyl, halogen, halo-lower alkyl, alkoxy, alkoxy-lower alkyl, halo-alkoxy, thioamido, amidosulfonyl, alkoxy carbonyl, carboxamide, aminocarbonyl, and alkylamino-carbonyl;

R₂ and R₃ are hydroxyl;

R₅ and R₆, when present, are selected from the group consisting of hydrogen, hydroxyl, alkoxy, carbonyl, alkoxy carbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl; and,

R₆ and R₆ are selected from the group consisting of hydrogen, hydroxyl, alkoxy, carboxyl, alkoxy carbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl,

with the proviso that Ring 1 is capable of binding to any of:

a dopaminergic receptor selected from the group consisting of a D1 receptor and a D5 receptor; a DAT transporter; a VMAT transporter; and,

with the proviso that E is capable of binding to a GLUT transporter selected from the group consisting of a GLUT1 receptor and a GLUT3 receptor.

2. (currently amended) The prodrug compound of claim 1, wherein the E substituent is selected from the group consisting of a radical of a monosaccharide, a disaccharide, a trisaccharide and an oligosaccharide.

3. (original) The prodrug compound of claim 1, wherein the E monosaccharide comprises a radical of a sugar selected from the group consisting of aldose, ketoaldose, alditols, ketoses,

aldonic acids, ketoaldonic acids, aldaric acids, ketoallic acids, amino sugars, keto-amino sugars, uronic acids, ketouronic acids, lactones and keto-lactones.

4. (currently amended) The prodrug compound of claim 3, wherein said radical of a sugar is ~~further~~ selected from the group consisting of triosyl, tetraosyl, pentosyl, hexosyl, heptosyl, octosyl and nonosyl radicals and derivatives thereof.

5. (original) The method of claim 4, wherein said pentosyl sugar radical comprises a straight carbon chain, a furanosyl ring or a derivative thereof.

6. (original) The prodrug compound of claim 4, wherein said hexosyl sugar radical comprises a straight carbon chain, a furanosyl ring, a pyranosyl ring or a derivative thereof.

7. (currently amended) The prodrug compound of claim 4, wherein said hexosyl radical is ~~further~~ selected from the group consisting of allose, altrose, glucose, mannose, gulose, idose, galactose, talose, fructose, ribo-hexulose, arabino-hexulose, lyxo-hexulose and derivatives thereof.

8. (currently amended) The prodrug compound of claim 4, wherein said pentosyl radical is ~~further~~ selected from the group consisting of ribose, arabinose, xylose, lyxose, ribulose, xylulose and derivatives thereof.

9. (currently amended) The prodrug compound of claim 4, wherein said heptosyl ~~residue~~ radical comprises sedoheptulose or a derivative and derivatives thereof.

10. (currently amended) The prodrug compound of claim 4, wherein said nonosyl ~~residue~~ radical comprises N-acetylneuraminic acid, N-glycolylneuraminic acid, diacetylneuraminic acid, or a derivative and derivatives thereof.

11. (currently amended) The prodrug compound of claim 7, further comprising glucose, galactose, fructose or a derivative derivatives thereof.

12. (currently amended) The prodrug compound of claim 2, wherein said disaccharide, trisaccharide ~~[[and]]~~ or oligosaccharide ~~comprise~~ comprises a sugar homopolymer or a sugar heteropolymer.

13. (currently amended) The prodrug compound of ~~claim 2~~ claim 12, wherein said sugar homopolymer comprises a glycoside selected from the group consisting of erythran, threan, riban, arabinan, xylan, lyxan, allan, altran, glucan, mannan, gulan, idan, galactan, talan, fructan or a derivative and derivatives thereof.

14. (currently amended) The prodrug compound of ~~claim 2~~ claim 12, wherein said sugar heteropolymer ~~further~~ comprises a glycoside selected from the group consisting of erythroside, threoside, riboside, arabinoside, xyloside, lyxoside, alloside, altroside, glucoside, mannoside, guloside, idoside, galactoside, taloside, fructoside or a derivative and derivatives thereof.

15. (currently amended) The prodrug compound of ~~claim 3~~ claim 13, wherein said glycoside ~~further~~ comprises a riban, an arabinan, a glucan, a galactan, a mannan or a derivative and derivatives thereof.

16. (currently amended) The prodrug compound of ~~claim 4~~ claim 13, wherein said glycoside ~~further~~ comprises a riboside, an arabinoside, a glucoside, a galactoside, a mannoside, a fructoside and derivatives thereof.

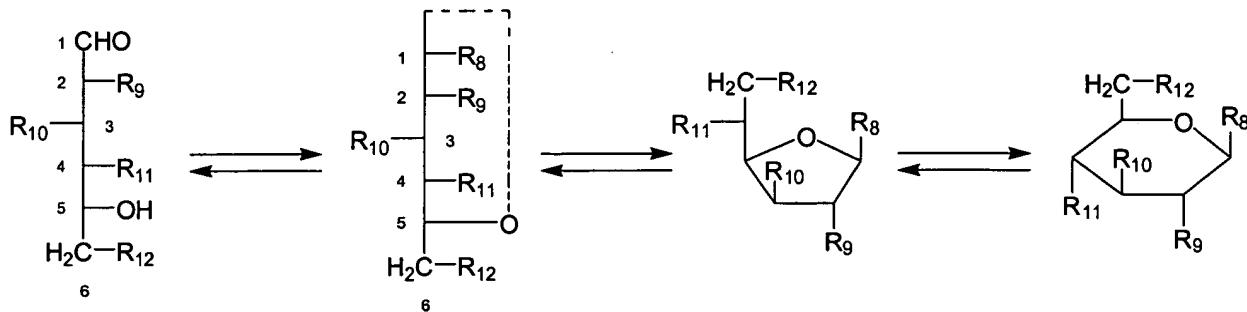
17. (currently amended) The prodrug compound of claim 15, wherein said glucan comprises maltose, amylose, glycogen, cellobiose, amylopectin, heparin or a derivative and derivatives thereof.

18. (currently amended) The prodrug compound of claim 16, wherein said glucoside comprises sucrose or a derivative and derivatives thereof.

19. (currently amended) The prodrug compound of claim 16, wherein said fructoside comprises fucosidolactose or a derivative and derivatives thereof.

20. (currently amended) The method of claim 16, wherein said galactoside comprises lactose, hyaluronic acid, pectin or a derivative and derivatives thereof.

21. (currently amended) The prodrug compound of claim 7, further comprising a sugar according to FORMULAS VIa, VIb, VIc and VId,



Formula VIa

Formula VIb

Formula VIc

Formula VIId

wherein R_8 , R_9 , R_{10} , R_{11} and R_{12} are selected from the group consisting of hydroxyl, hydrogen, hydroxyl, methyl, lower alkyl, halogen, halo-lower alkyl, alkoxy, alkoxy, ketone, carboxyl, amine, amido, N-acetyl, N-methyl, N-linked lower alkyl, aminocarbonyl, alkylaminocarbonyl, dialkylaminocarbonyl, and phosphate, sulfate and thiol.

22. (currently amended) The prodrug compound of claim 1, further comprising a wherein the compound that binds to dopamine receptor in a mammalian cell.

23. (currently amended) The prodrug compound of claim 1, further comprising a wherein the compound that binds to and is transportable by a DAT transporter in a neural cell.

24. (currently amended) The prodrug compound of claim 1, further comprising a wherein the compound that binds to and is transportable by a GLUT transporter in a neural cell or a vascular endothelial cell.

25. (currently amended) The prodrug compound of claim 1, further comprising a wherein the compound is transportable at the blood brain barrier by an endothelial cell.

26. (currently amended) A dopaminergic pharmaceutical composition comprising: one or more of an additive, a stabilizer, a carrier, a binder, a buffer, an excipient, a filler, an emollient, a disintegrant, a lubricating agent, [[and]] or a antimicrobial agent; and, a hydrophilic transportable dopaminergic prodrug compound according to claim 1.

27. (original) The dopaminergic pharmaceutical composition of claim 26, further comprising a form suitable for dermal administration, oral administration, buccal administration, trough administration, parenteral administration, injection, intra-rectal administration, intrathecal administration, intra-nasal administration, intra-bronchial administration and intra-ocular administration.

28. (currently amended) The dopaminergic pharmaceutical composition of claim 27, wherein said form is selected from the group consisting of a syrup, an elixir, a tablet, a lozenge[[r]], a capsule, a perenteral solution, an injection solution, a nasal solution, an eye drops solution, a powder, a granule, a timed-release capsule, an emollient cream, a salve, an ointment, an impregnated bandage, a timed-release lipid soluble patch, a trough and a suppository.

29. (currently amended) A method for preparing a pharmaceutical composition comprising the step of adding one or more of an additive[[s]], a stabilizers, a carrier[[s]], a binder[[s]], a buffer[[s]], an excipient[[s]], a filler[[s]], an emollient[[s]], a disintegrant[[s]], a lubricating agent[[s]], or a antimicrobial agent[[s]] to a hydrophilic transportable dopaminergic prodrug compound according to claim 1.

30. (original) A hydrophilic prodrug dopaminergic pharmaceutical composition for metabolic replacement therapy in a subject with Parkinson's disease or a Parkinson's related disease comprising a compound according to FORMULA I:

A-B-D-E

Formula I

wherein,

A, comprises a cyclic, heterocyclic, aryl or heteroaryl ring capable of binding to both a dopamine receptor and a dopamine transporter in a neural cell; B, comprising a bridging lower alkyl moiety linked through single bonds with each of A and D; D, comprises an amide or an amine linked through single bonds with each of B and E; E, comprises a saccharide moiety; and,

said compound according to FORMULA I binds to and is transportable by a GLUT in a blood cell; binds to and is transportable by a GLUT in a vascular endothelial cell; binds to and is transportable by a DAT; and is capable of binding to a dopamine receptor in a neural cell.

31. (original) A method for treating a dopaminergic transcription regulatory defect in a subject in need thereof, comprising the step of administering to the subject a compound effective to bind both a GLUT and a DAT in a neural cell, wherein the activation of the GLUT or the DAT is effective to alter the transcription of a dopaminergic gene in the neural cell, wherein the dopaminergic gene is selected from the group consisting of a tyrosine hydroxylase gene, an aromatic decarboxylase gene, a monoamine oxidase gene, a DAT gene, a VMAT2 gene, a Nurr1 or a Nurr2 gene, and SP1 or SP3 gene, a dopaminergic receptor gene, a synuclein gene, and Elk gene, a Hic-5 gene, and Lmx1b gene, a Pitx3 gene, a HoxA5 gene, a HNF-3 β gene and a HoxA4 gene.

32. (currently amended) A method for identifying a candidate drug substance for treating a dopaminergic transcription regulatory defect, comprising the steps of:

measuring binding or transport of a test compound by a GLUT or by a DAT transporter;
measuring transcription of a dopaminergic gene selected from the group consisting of a tyrosine hydroxylase gene, an aromatic decarboxylase gene, a monoamine oxidase gene, a DAT gene, a VMAT2 gene, a Nurr1 or a Nurr2 gene, and SP1 or SP3 gene, a dopaminergic receptor gene, a synuclein gene, and Elk gene, a Hic-5 gene, and Lmx1b gene, a Pitx3 gene, a HoxA5 gene, a HNF-3 β gene and a HoxA4 gene; **and**

determining that the test compound is the candidate drug substance if the test compound is bound or transported by either of the GLUT or the DAT transporters and that the transcription of the dopaminergic gene is increased or decreased relative to a vehicle treated negative control.

33. (original) The method of claim 32, wherein the test compound is transported by a GLUT3 transporter.

34. (original) The method of claim 32, wherein the test compound increases the transcription of a tyrosine hydroxylase gene.

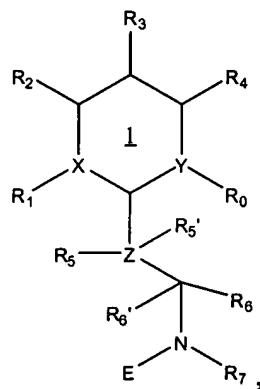
35. (original) The method of claim 32, wherein the test compound decreases the transcription of an alpha-synuclein gene.

36. (original) The method of claim 32, wherein the test compound increases the transcription of a Nurr gene.

37. (original) The method of claim 36, wherein the increased mRNA transcript of the Nurr1 gene is Nurr1 or Nurr2.

38. (original) A method for treating a tyrosine hydroxylase genetic defect in a subject in need thereof, comprising the step of administering to the subject a pharmaceutical compound transportable by both a GLUT-3 transporter and a DAT transporter in a manner effective to increase transcription of the tyrosine hydroxylase gene in the subject.

39. (new) A compound having the formula



wherein

- Ring 1 is an optionally substituted aryl ring;

- b) X and Y are carbon atoms;
- c) R₀ is hydrogen;
- d) R₃ is hydroxyl;
- e) R₁, R₂ and R₄ are independently selected from the group consisting of hydrogen, hydroxyl, halogen, halo-lower alkyl, alkoxy, alkoxy-lower alkyl, halo-alkoxy, thioamido, amidosulfonyl, alkoxy carbonyl, carboxamide, amino-carbonyl, and alkylamine-carbonyl;
- f) z is absent or a carbon atom;
- g) R₅, R_{5'}, R₆ and R_{6'} are independently selected from the group consisting of hydrogen, hydroxyl, alkoxy, carboxyl, alkoxy carbonyl, aminocarbonyl, alkylamino-carbonyl and dialkylamino-carbonyl;
- h) N is the nitrogen atom of a primary or secondary amine or an amide;
- i) R₇ is a hydrogen or methyl; and
- j) E is a sugar residue having 3, 4, 5, 6, 7, 8, or 9 carbon atoms,
or a pharmaceutically acceptable salt thereof.

40. (new) The compound of claim 39, wherein N is the nitrogen atom of an amide.

41. (new) The compound of claim 39, wherein N is the nitrogen atom of a primary or secondary amine.

42. (new) The compound of claim 39, wherein z is a carbon atom.

43. (new) The compound of claim 39, wherein R₇ is a hydrogen.

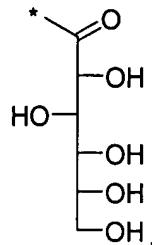
44. (new) The compound of claim 39, wherein R₂ is hydroxyl.

45. (new) The compound of claim 39, wherein R₅ or R_{5'} is hydroxyl.

46. (new) The compound of claim 39, wherein the sugar residue is straight chained.

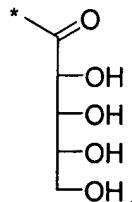
47. (new) The compound of claim 46, wherein the sugar is a straight chain hexose sugar.

48. (new) The compound of claim 39, wherein the sugar residue comprises the structure:



49. (new) The compound of claim 39, wherein E is produced from gluconolactone.

50. (new) The compound of claim 39, wherein the sugar residue comprises the structure:



51. (new) The compound of claim 39, wherein E is produced from D-(+)-ribonic acid gamma-lactone.

52. (new) The compound of claim 39, wherein:

- a) R₁, R₄, R₅, R_{5'}, R₆, R_{6'} and R₇ are hydrogen,
- b) R₂ is hydroxyl,
- c) z is a carbon atom, and
- d) E is a residue of a straight chain hexose sugar.

53. (new) The compound of claim 39, wherein:

- a) R₁, R₂, R₄, R₅, R₆, R_{6'} and R₇ are hydrogen,
- b) R_{5'} is hydroxyl,
- c) z is a carbon atom, and
- d) E is a residue of a straight chain hexose sugar.

54. (new) A pharmaceutical composition comprising one or more compounds of claim 39 and a formulary agent in a dosage form suitable for administration to man or a domestic animal.

55. (new) Dopamine gluconamide or a pharmaceutically acceptable salt thereof.

56. (new) A process for making the dopamine gluconamide of claim 55 or the pharmaceutically acceptable salt thereof, the process comprising the steps of:

- a) reacting gluconolactone and 3-hydroxytyramine, and
- b) collecting the dopamine gluconamide or the pharmaceutically acceptable salt thereof.

57. (new) A method for treating Parkinson's disease in a subject diagnosed with a need thereof, comprising the step of administering to the subject the dopamine gluconamide of claim 55 or the pharmaceutically acceptable salt thereof in an amount effective to treat the Parkinson's disease in the subject.

58. (new) Dopamine gluconamine or a pharmaceutically acceptable salt thereof.

59. (new) A process for making the dopamine gluconamine of claim 58 or the pharmaceutically acceptable salt thereof, the process comprising the steps of:

- a) providing dopamine gluconamide,
- b) protecting the aromatic hydroxyl groups of the dopamine gluconamide, and
- c) reducing the protected dopamine gluconamide to form the dopamine gluconamine or the pharmaceutically acceptable salt thereof.

60. (new) A method for treating Parkinson's disease in a subject diagnosed with a need thereof, comprising the step of administering to the subject the dopamine gluconamine of claim 58 or pharmaceutically acceptable salt thereof in an amount effective to treat the Parkinson's disease in the subject.

61. (new) Dopamine ribonamide or a pharmaceutically acceptable salt thereof.

62. (new) Dopamine ribonamine or a pharmaceutically acceptable salt thereof.

63. (new) A process for preparing a dopamine amide comprising:

- a) reacting a lactone of a sugar and 3-hydroxytyramine, and
- b) collecting the dopamine amide.

64. (new) The process of claim 63, wherein the lactone of a sugar is gluconolactone.

65. (new) The process of claim 63, wherein the lactone of a sugar is D-(+)-ribonic acid.

66. (new) A dopamine amide produced by the process of claim 63.

67. (new) A process for preparing a dopamine amine comprising:

- a) providing a dopamine amide,
- b) protecting the aromatic hydroxyl groups of the dopamine amide, and
- c) reducing the protected dopamine amide to form dopamine amine.

68. (new) The process of claim 67, wherein the dopamine amide is dopamine gluconamide

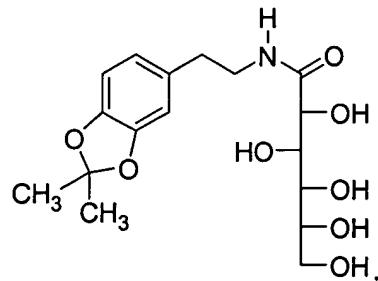
69. (new) The process of claim 67, wherein the dopamine amide is dopamine ribonamide.

70. (new) The process of claim 67, wherein the dopamine amide is dopamine gluconamine

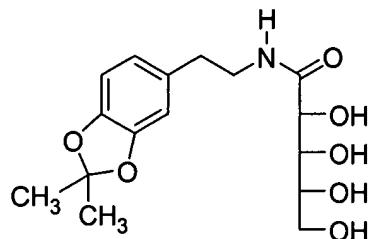
71. (new) The process of claim 67, wherein the dopamine amide is dopamine ribonamine.

72. (new) The process of claim 67, wherein the protection of the aromatic hydroxyl groups occurs by condensation of the dopamine amide with acetone to form a isopropylidene-protected dopamine amide.

73. (new) The process of claim 72, wherein the isopropylidene-protected dopamine amide has the structure:



74. (new) The process of claim 72, wherein the isopropylidene-protected dopamine amide has the structure:



75. (new) A dopamine amine produced by the process of claim 67.